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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

GARCIA, M

ART UNIT

PAPER NUMBER

1627
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File copy

Office Action Summary

Application No.
09/457,926

Applicant(s)

Christensen et al

Examiner
Maurie E. Garcia, Ph. D.

Art Unit
1627



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE THREE MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Mar 19, 2001

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 41-56 is/are pending in the application.

4a) Of the above, claim(s) 42, 44-46, 50, 51, and 56 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 41, 43, 47-49, and 52-55 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirements.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

- ☐ Certified copies of the priority documents have been received.
- ☐ Certified copies of the priority documents have been received in Application No. _____.
- ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

19) ☐ Notice of Informal Patent Application (PTO-152)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 & 11-13

20) ☐ Other:

DETAILED ACTION

1. The Response filed March 19, 2001 (Paper No. 10) is acknowledged. No claims were cancelled, added or amended. Therefore, claims 41-56 are pending.

Election/Restriction

2. Applicant's election with traverse of Group I (claims 41-55) and election of species is also acknowledged. The traversal is addressed below.

3. On pages 2-3 of the Response, applicants traverse the Restriction Requirement with respect to the separation of the claims of Group I from Group II and state that combined search and examination would not create an undue burden. However, the examiner maintains that the inventions are distinct since the compounds of Group I could be used in a variety of different methods, such as diagnostic methods. Again, as stated in the Restriction Requirement, there is no expectation that the searches of these two groups would be coextensive. Therefore, this does create an undue search burden. The requirement is still deemed proper and is therefore made FINAL.

4. Applicant's election of species in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement with respect to the species election, the election has been treated as an election without traverse (MPEP § 818.03(a)).

5. Claim 56 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 10. Claims 42, 44-46, 50 and 51 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to non-elected species. Election was made **without** traverse in Paper No. 10 for the species (see above).

6. Therefore, claims 41, 43, 47-49 and 52-55 are examined on the merits.

Information Disclosure Statement

7. The information disclosure statement filed September 13, 2000 fails to *fully* comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent, publication, or other information listed that is not in the English language. It has been placed in the application file, but the information referred to therein with respect to the document EP 322810 has not been considered. The patent is not in English and no English language Abstract or any other documentation was provided.

Specification

8. The abstract of the disclosure is objected to because it is two paragraphs. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Please note that there are two separate issues under 35 U.S.C. 112, first paragraph.

These are set forth below in separate rejections for clarity.

Linker structure

11. Claims 41, 43, 47-49 and 53-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

There are a virtually unlimited number of compounds that would fall within the claimed genus of compounds utilizing the claimed ligands. This is because the instant claims give *no structure* of the linker moiety (X). Thus the instant claims could encompass an infinite number of variations. However, the instant description discloses the preparation of only a very limited number of such compounds.

The present application fails to describe sufficient examples of linked ligands that are within the scope of the presently claimed invention. The instant description discloses the preparation of only a very limited number of compounds. The instant description also discloses only a limited number of examples of how the instant “ligands” can be linked together to form multimeric compounds. Applicant’s claimed scope represents only an invitation to experiment regarding possible compounds.

With respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding disclosure. For adequate disclosure, like enablement, requires *representative examples* which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention*. See *In re Riat et al.* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr et al.* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by “representative examples”) for both enablement and adequate disclosure.

Thus, the disclosure is neither representative of the claimed genus, which encompasses any compound comprising the claimed ligands linked with any

linker, nor does it represent a substantial portion of the claimed genus. Moreover, the claimed genus encompasses members which are yet to be prepared or envisioned. This further evidences that the structural features of the exemplified compounds do not constitute support for the claimed genus or a substantial portion thereof.

12. Claims 41, 43, 47-49 and 53-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific compounds where structures of the linker moiety are shown, does not reasonably provide enablement for any compound utilizing the claimed ligands linked with *any* linker. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is clear from applicant's specification how one might practice this invention with specific compounds where structures, linkage sites and linkers are shown; however, there is insufficient guidance as to how to make/use any compound utilizing the claimed ligands linked with *any* linker. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to:

- (1) the breadth of the claims;
- (2) the nature of the invention;

- (3) the state of the prior art;
- (4) the level of one of ordinary skill;
- (5) the level of predictability in the art;
- (6) the amount of direction provided by the inventor;
- (7) the existence of working examples; and
- (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: The claims are drawn to a compound utilizing the claimed ligands that are linked with a linker. No other structural limitations on the structure of the linker are given and, as such, this could read on a wide variety of structures. Such represents broad scope.

(3 and 5) The state of the prior art and the level of predictability in the art: Multimeric compounds and methods for linking such were known at the time of filing; however, only limited numbers of such compounds were known and the specification gives no guidance to permit one of skill in the art to devise strategies for synthesis of any multibinding compound utilizing the claimed ligands linked with *any* linker. The structures of possible variants are sufficiently diverse and one of ordinary skill would not be able to predict such structures. Applicant's claimed scope of compounds represents only an invitation to experiment regarding possible compounds (see also above concerning written description and cases cited therein). See also rejection under 35 USC 112, second paragraph below.

(4) The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants have only provided examples of certain multimeric compounds that consist of ligands with defined linkage sites and defined linkers. However, no generic strategy for determining linker structure is given. One of ordinary skill could not guess, *a priori*, how to make and use compounds that are made from ligands with undefined linkers. It appears that the claims omit matter disclosed to be essential to the invention. The instant specification describes the claimed compounds as being able to bind in a multivalent manner due to their structure (see instant specification, page 34, line 7 through page 36, line 4 and elsewhere) which is interpreted as meaning that the ligands must be linked in some defined way for the invention to function as intended. Claims 41, 43, 47-49 and 53-55 disclose no information on the structure of the linker moiety. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976) regarding omission of essential matter and see also MPEP § 2164.08(c).

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: In claims 41, 43, 47-49 and 53-55 there is only the broad recitation that the claimed compounds contain ligands (L) linked by a linker (X). However, the instant specification gives one skilled in the art no indication of how to make and use such compounds as the structure of the linkers are not defined. Thus, one of ordinary skill would not have a reasonable expectation of success. Therefore, further research would be necessary to make

or use the invention as claimed and the practice of the full scope of the invention would require undue experimentation.

Any glycopeptide antibiotic

13. Claims 41, 43, 47, 48, 52 and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for vancomycin as the glycopeptide antibiotic, does not reasonably provide enablement for any glycopeptide antibiotic. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is clear from applicant's specification how one might practice this invention when the glycopeptide antibiotic is vancomycin; however, there is insufficient guidance as to how to make/use **any** glycopeptide antibiotic. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue".

These factors include, but are not limited to:

- (1) the breadth of the claims;
- (2) the nature of the invention;
- (3) the state of the prior art;
- (4) the level of one of ordinary skill;
- (5) the level of predictability in the art;
- (6) the amount of direction provided by the inventor;
- (7) the existence of working examples; and
- (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: The claims simply state that one ligand is a glycopeptide antibiotic (optionally substituted) or aglycon derivative thereof. No other limitations on this ligand are given and, as such, this could read on a wide variety of structures. Such represents very broad scope.

(3 and 5) The state of the prior art and the level of predictability in the art: Glycopeptide antibiotics were known at the time of filing; however, these compounds are very complex in structure and *general* synthetic schemes for such compounds were not well known. Most importantly, glycopeptide antibiotics have many sites for potential reaction (linkage) and these sites have the potential for cross-reaction (i.e. may need protecting groups, etc.). The structures of possible variants (linkage sites) are sufficiently diverse and one of ordinary skill would not be able to predict their reactivity. Only for vancomycin is the chemistry well defined enough to be carried out without undue experimentation. See Nicolaou et al Angew. Chem. Intl. Ed. 1999, Vol. 38, pp. 2096-2152 in general, especially page 2109, 2nd column.

(4) The level of one of ordinary skill: The level of skill would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: The specification gives no guidance to permit one of skill in the art to devise strategies for linkage chemistry of *any* glycopeptide antibiotic. Applicants have only provided working examples of vancomycin as the

glycopeptide antibiotic; therefore further research would be necessary to make or use the invention for any other glycopeptide antibiotic. Applicant's claimed scope represents only an invitation to experiment regarding possible compounds.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: In claims 41, 43, 47, 48, 52 and 55 there is no limitation recited on the type of glycopeptide antibiotic used in the compound. However, the instant specification gives one skilled in the art **no** indication that one could use *any* glycopeptide antibiotic and have a reasonable expectation of success. Therefore, the practice of the full scope of the invention would require undue experimentation.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 41, 43, 47-49 and 53-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 41, 43, 47-49 and 53-55 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural

cooperative relationships are: the structure of the linkers. Thus, one of ordinary skill would not know the metes and bounds of the claimed invention. See also rejections under 112, first paragraph above (paragraphs 11 & 12).

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

(f) he did not himself invent the subject matter sought to be patented.

17. Claims 41, 43, 47-49 and 52-55 are provisionally rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 09/317,198 which has a common inventor with the instant application.

Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e), if patented. This provisional rejection under 35 U.S.C. 102(e) is based upon a presumption of future patenting of the copending application.

The instant claims 41, 43, 47-49 and 52-55 are drawn to compounds that are disclosed in application 09/317,198. See pending claims in the '198 application and the disclosure, especially Examples and Figures 6B and 9.

This provisional rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not

claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

NOTE: This rejection may not be overcome by the filing of a terminal disclaimer. See *In re Bartfeld*, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991).

18. Claims 49 and 55 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

The instant claims 49 and 55 claim the exact same invention as claims 50 and 55 of application 09/317,198. However, the two applications do not have the same inventive entity. Thus it appears that there is a question as to the inventor of this subject matter. See also paragraphs 22-25 below.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

20. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under

37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

21. Claims 41, 43, 47-49 and 52-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Truett (US 5,693,791; on PTO-1449) in view of Boeckh et al (Antimicrob. Agents Chemother., 1988, Vol. 32, No. 1, pp. 92-95).

Truett teaches the “linking of diverse antibiotic moieties via difunctional organic compounds” (see column 1, lines 8-9). Specifically, dimers are taught having the structure A-L-B, where A and B are various antibiotic moieties (see “Summary”, columns 1-6, especially column 1, lines 46-64). A variety of linkers and linkage chemistries are taught (see columns 25-32). The reference teaches that the linkage of two antibiotic moieties can create compounds of new activity (see column 1, lines 1-30) and that “two antibiotic moieties can be linked in which one is known to attack Gram positive bacteria and another to attack Gram negative bacteria” (see column 1, lines 27-30). Truett teaches a dimeric compound where one of the antibiotic moieties is ceftazidime (see column 3, line 7). Ceftazidime is a beta lactam antibiotic that reads on the elected species that is set forth in claim 53, see structure in the instant Figure 6B-2. Truett lacks the teaching of linking vancomycin with ceftazidime.

However, it was well known in the art at the time of filing to use combination therapy with vancomycin and ceftazidime. Boeckh et al teach that this combination therapy is used to "cover a broad spectrum of gram positive and gram negative bacteria" (see page 92, 1st paragraph). The reference teaches the pharmacokinetics of the combination of vancomycin and ceftazidime, administered to humans (see Abstract and Table 1), thus pharmaceutical compositions of the drugs are well known.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to link vancomycin and ceftazidime, based on the teaching of Boeckh et al to perform combination therapy using the drugs, and the teaching of Truett concerning the linking of diverse antibiotic moieties. Specifically, Truett teaches that two antibiotics, one known to attack Gram positive bacteria and another to attack Gram negative bacteria can be linked, and Boeckh et al teach that vancomycin and ceftazidime fulfill these requirements. One would have been motivated to do so to create a broad spectrum antibiotic compound.

Double Patenting

22. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject

matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

23. A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

24. Claims 49 and 55 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 50 and 55 of copending Application No. 09/317,198. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

25. Claims 49 and 55 are directed to the same invention as that of claims 50 and 55 of commonly assigned 09/317,198. The issue of priority under 35 U.S.C. 102(g) and possibly 35 U.S.C. 102(f) of this single invention must be resolved. Since the Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302), the assignee is required to state which entity is the prior inventor of the conflicting subject matter. A terminal disclaimer has no effect in this situation since the basis for refusing more than one patent is priority of invention under 35 U.S.C. 102(f) or (g) and not an extension of

monopoly. *Failure to comply with this requirement will result in a holding of abandonment of this application.*

26. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

27. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

28. Claims 41, 43, 47, 48 and 52-54 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 43-49, 53, 54 and 57-61 of copending Application No. 09/317,198. Although the

conflicting claims are not identical, they are not patentably distinct from each other because the recited claims in each application encompass embodiments (species of ligands) that are the same. Thus, the Markush groups of ligands in each of the recited cases have overlapping members and the compounds encompassed by the claims in each of the applications could be the same. The scope in each application is only slightly different. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Status of Claims/Conclusion

29. **Please note:** The provisional rejection under 35 U.S.C. 102(e), rejection under 35 U.S.C. 102(f) and all double patenting rejections are based ONLY on the examined claims (see paragraph 6 above). The examiner would like to point out that there are other claims that were withdrawn from consideration (drawn to non-elected species) that would most likely fall within these rejections as well. These issues will be addressed if/when those claims are examined on the merits.

30. No claims are allowed.

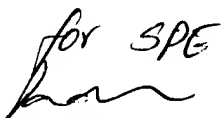
31. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A. Sundram et al. J. Org. Chem., 1995, Vol. 60, pp. 1102-1103. The reference teaches covalent modification of vancomycin (see Figure 1).

- B. Sundram et al. J. Am. Chem. Soc., 1996, Vol. 118, pp. 13107-13108. The reference teaches synthesis of vancomycin dimers (see Figure 1).
- C. Rao et al. J. Am. Chem. Soc., 1997, Vol. 119, pp. 10286-10290. The reference teaches synthesis of vancomycin dimers and general tenets of divalency (see Schemes 1 and 2).

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie E. Garcia, Ph.D. whose telephone number is (703) 308-0065. The examiner can normally be reached on Monday-Thursday from 8:30 to 6:00 and alternate Fridays.

33. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

for SPE

PADMASHRI PONNALURI
PRIMARY EXAMINER

Maurie E. Garcia, Ph.D.
June 4, 2001